

U.S.S.N. 09/687,483
BRAUN *et al.*
AMENDMENT

IN THE CLAIMS

Please cancel claims 30, ~~51~~, 52, 60-64, 71-81, and 83-85 without prejudice or disclaimer.

Please replace claims 4, 8, 9, 43, 53, 54 and 100 with amended claims 4, 8, 9, 43, 53, 54 and 100 as follows:

D2

4. (Amended) A method of producing a database, comprising:
identifying healthy members of a population;
obtaining data comprising identifying information and obtaining historical information and data relating to the identified members of the population and their immediate family;

entering the data for each member of the population into a database;
associating the respective data of the individual member with an indexer;
and

storing the database on a computer-readable medium.

5. (Amended) The method of claim 4, further comprising:
obtaining a body tissue, body fluid sample, or other biological sample;
analyzing the body tissue, body fluid, or biological sample; and
entering the results of the analysis for each member into the database
and associating each result with the indexer representative of each member.

D3

8. (Amended) A database, comprising:
datapoints representative of a plurality of healthy organisms from whom biological samples are obtained; and

an indexer that identifies each organism, wherein
a) each datapoint is associated with data representative of the organism type and other identifying information by the indexer; and

b) the database is stored on a computer-readable medium; and

c) the database is sortable.

9. (Amended) The database of claim 8, wherein the datapoints comprise answers to questions regarding one or more parameters selected from the group consisting of ethnicity, age, gender, height, weight, alcohol intake,

U.S.S.N. 09/687,483
BRAUN *et al.*
AMENDMENT

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number of pregnancies, number of live births, vegetarianism, type of physical activity, state of residence and/or length of residence in a particular state, educational level, age of parent at death, cause of parent death, former or current smoker, length of time as a smoker, frequency of smoking, occurrence of a disease in immediate family (parent, siblings, children), use of prescription drugs and/or reason therefor, length and/or number of hospital stays, and exposure to environmental factors.

43. (Amended) A method of producing a database stored in a computer memory, comprising:

D4
identifying healthy members of a population;

obtaining identifying and historical information and data relating to the identified members of the population;

entering the member-related data into the computer memory database for each identified member of the population and associating the member and the data with an indexer, wherein the database is a relational database.

D5
53. (Amended) A computer system, comprising the database of claim 50.

54. (Amended) An automated process line, comprising the database of claim 50.

D6
100. (Amended) A system for high throughput processing of biological samples, comprising:

an automated process line comprising a plurality of processing stations, each of which performs a procedure on a biological sample contained in a reaction vessel;

a database of claim 8, wherein the samples tested by the automated process line comprise samples from subjects in the database; and

a mass spectrometer for analysis of biopolymers in the samples.

U.S.S.N. 09/687,483
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AMENDMENT

Please add new claims 101-108.

101. (New) A method for high throughput processing of biological samples, the method comprising:

transporting a reaction vessel along a system of claim 32, comprising a process line having a plurality of processing stations, each of which performs a procedure on one or more biological samples contained in the reaction vessel;

determining when the test procedure at each processing station is complete and, in response, moving the reaction vessel to the next processing station;

receiving test results of the process line and automatically processing the test results to make a data analysis determination regarding the biological samples in the reaction vessel; and

processing reaction vessels continuously one after another until receiving a stop instruction, wherein the samples tested by the automated process line comprise samples from subjects in the database.

102. (New) The method of 101, wherein one of the processing stations comprises a mass spectrometer.

103. (New) The method of claim 102, wherein the samples are analyzed by a method comprising primer oligo base extension (PROBE).

104. (New) The method of claim 103, further comprising:

processing the test results by receiving test data from the mass spectrometer such that the test data for a biological sample contains one or more signals or numerical values representative of signals, whereupon the data analysis system determines the area under the curve of each signal and normalizes the results thereof and obtains a substantially quantitative result representative of the relative amounts of components in the tested sample.

105. (New) The method of claim 103, wherein primer oligo base extension (PROBE) comprises:

U.S.S.N. 09/687,483

BRAUN *et al.*

AMENDMENT

- a) obtaining a nucleic acid molecule that contains a target nucleotide;
- b) optionally immobilizing the nucleic acid molecule onto a solid support, to produce an immobilized nucleic acid molecule;
- c) hybridizing the nucleic acid molecule with a primer oligonucleotide that is complementary to the nucleic acid molecule at a site adjacent to the target nucleotide;
- d) contacting the product of step c) with composition comprising a dideoxynucleoside triphosphate or a 3'-deoxynucleoside triphosphates and a polymerase, so that only a dideoxynucleoside or 3'-deoxynucleoside triphosphate that is complementary to the target nucleotide is extended onto the primer; and

e) detecting the primer, thereby identifying the target nucleotide.

106. (New) The method of 105, wherein detection of the extended primer is effected by mass spectrometry, comprising:

ionizing and volatilizing the product of step d); and

detecting the extended primer by mass spectrometry, thereby identifying the target nucleotide.

107. (New) The method of claim 102, wherein the target nucleic acids in the sample are detected and/or identified by a method, comprising the steps of:

- a) hybridizing a first oligonucleotide to the target nucleic acid;
- b) hybridizing a second oligonucleotide to an adjacent region of the target nucleic acid;
- c) ligating then hybridized oligonucleotides; and
- d) detecting hybridized first oligonucleotide by mass spectrometry as an indication of the presence of the target nucleic acid.

108. (New) The method of claim 102, wherein the target nucleic acids in the sample are detected and/or identified by a method, comprising the steps of: